UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,466	01/16/2001	Ike W. Lee	01948/069002	5761

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EXAMINER
QIAN, CELINE X

ART UNIT	PAPER NUMBER
2656	16

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Please find below and or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/761,466	LEE ET AL.
	Examiner	Art Unit
	Celine X Qian	1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,9,11,12 and 18-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,9,11,12 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other

DETAILED ACTION

Claims 1-6, 8, 9, 11, 12 and 18-20 are pending in the application.

Claims 7, 10 and 13-17 are cancelled. Claims 1-6, 8, 9, 11, 12 and 18-20 are currently under examination.

This Office Action is in response to the Amendment filed on 12/23/02.

Response to Amendment

The rejection of claim 11 under 35 U.S.C. 102 (b) has been withdrawn in light of Applicants' amendment of the claims.

The rejection of claim 8 under 35 U.S.C. 112 first paragraph (enablement) has been withdrawn in light of Applicants' amendment of the claims.

Claims 1-6, 8, 9, 11, 12 and newly added claims 18-20 stand rejected under 35 U.S.C. 112 second paragraph for reasons set forth of the record mailed on 7/16/02 and further discussed below.

Claims 1-6, 8, 9, 11, 12 and newly added claims 18-20 stand rejected under 35 U.S.C. 112 first paragraph (written description) for reasons set forth of the record mailed on 7/16/02 and further discussed below.

Claims 1-6, 9, 11, 12 and newly added claims 18-20 stand rejected under 35 U.S.C. 112 first paragraph (enablement) for reasons set forth of the record mailed on 7/16/02 and further discussed below.

Newly added claims 18 and 20 are rejected under 35 U.S.C. 112 second paragraph for reasons discussed below.

Response to Arguments

Claim Rejections - 35 USC § 112 First paragraph

In response to the written description rejection, Applicants argue that the amended claims now requires a nucleic acid sequence having at least 90% sequence identity to the full length sequence of both SEQ ID NO:1 and SEQ ID NO:2 in which both region A1 and A2 are present. Applicants also argue that claim 11 has been amended to recite a polynucleotide having at least 90% sequence identity to SEQ ID NO:4 which also comprises both A1 and A2. Applicants further argue such amendment also requires the presence of a nucleotide sequence having at least 90% sequence identity to both A1 and A2. Therefore, such amendment overcomes the written description rejection.

The above arguments has been considered but deemed not persuasive. The amended claims recite nucleic acids having 90% homology to SEQ ID NO:1 and SEQ ID NO: 2, SEQ ID NO:3, SEQ ID NO: 4, or 80% homology to SEQ ID NO:6, which encompass a vast genus of nucleic acids of different sizes (the claims recites "comprise") having these sequence homologies. Claim 8 encompasses any nucleic acid molecules having cardiac specific enhancer activity and comprising at least three transcription factor binding sites. The specification only discloses that 3 isolated nucleic acids (1kb to 20kb) spanning A1+A2 (SEQ ID NO:1 & 2) regions have cardiac enhancer activity, wherein A1+A2 region comprises transcription binding sites such as Mef2, dHAND, GATA and TGF-β. The specification does not teach nucleic acids sharing 90% homology with both A1 and A2 having cardiac specific enhancer function. The specification also fails to teach nucleic acids having 90% homology with SEQ ID NO: 3 or 4 having cardiac specific enhancer function, or nucleic acids having 80% homology with SEQ ID

NO 6 having a repressor function. The specification does not teach other nucleic acids (besides A1 and A2 and the 7 5kb, 20kb fragment that comprises A1 and A2) that comprise three transcription factor binding sites as recited in claim 8 which have cardiac specific enhancer activity. The specification does not teach which specific nucleotide within A1 and A2 is essential for the enhancer function. Moreover, the specification fails to teach which specific nucleotide within SEQ ID NO 6 having repressor function. Without such information, the structural and functional relationship between the claimed nucleic acid sequences and their function either as cardiac specific enhancer or repressor is missing. The specification neither describes a representative number of species of the invention by their complete structure nor other relevant identifying characteristics. Therefore, the written description requirement is not met, and the rejection is maintained.

Claims 18-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The newly added claims 19-20 also encompass a vast genus of nucleic acids of different sizes (the claims recites "comprise") having these sequence homologies either 90% to SEQ ID NO:3, 95% to SEQ ID NO:1 & 2, or 95% to SEQ ID NO:3. The specification does not teach nucleic acids having 90-95% homology with SEQ ID NO:3, or 95% to SEQ ID NO:1 & 2 having cardiac specific enhancer activity. For same reason discussed above, the specification fails to describes a representative species of the invention by neither their complete structure nor other relevant identifying characteristics. Therefore, the written description requirement is not met.

In response to the enablement rejection, Applicants argue that the nucleic acids recited in amended claims can be readily tested for its function as a cardiac enhancer or repressor according to the teachings of the specification. Applicants argue that one skilled in the art could readily clone a polynucleotide sequence sharing at least 90% sequence identity to either SEQ ID NO:1 and 2, or SEQ NO:4 into a reporter construct and measure the activity of the reporter, thus determine if the polynucleotide sequence having enhancer or repressor activity without undue experimentation. Applicants further argue that claim 8 as amended is fully enabled because the Examiner fails to provide evidence that the recited cardiac enhancer would be functional

Applicants' argument have been fully considered but deemed unpersuasive. The amended claims recite nucleic acids having 90% homology to SEQ ID NO:1 and SEQ ID NO: 2, SEQ ID NO:3, SEQ ID NO: 4, or 80% homology to SEQ ID NO:6, which encompass a great number of nucleic acids of different sizes. The examiner agrees that cloning those nucleic acids and testing for their function would not be undue experimentation based on the teaching of the specification, however, one skilled in the art would not know how to use a nucleic acid having 90% homology with SEQ ID NO:1 & 2 without cardiac enhancer function based on the instant specification. To satisfy the enablement requirement, the specification needs to teach both how to make and use the claimed nucleic acids without undue experimentation.

As discussed in the previous office action, the specification does not teach which specific nucleotide within A1 and A2 is essential for the enhancer function. Moreover, the specification fails to teach which specific nucleotide within SEQ ID NO:6 having repressor function. The art teaches that specific transcriptional factor binding element(s) is critical for a specific promoter/enhancer/repressor function. Deleting or mutating of these critical elements (rather

than the nucleotides flanking these elements) often renders the promoter/enhancer/repressor non-function. Whether nucleic acid having 90%-95% sequence homology with full length SEQ ID 1, 2, 3 or 4, wherein it does not share homology with these critical element(s) can retain its cardiac specific enhancer or repressor activity is unpredictable. In addition, the claims encompass a great number of nucleic acids of different sizes. Without knowing any information of the rest of the nucleic acid sequence (besides a certain portion having homology to sequences having cardiac specific enhancer or repressor activity), whether it can retain the enhancer activity or repressor activity is unpredictable. The remaining sequence may comprise other enhancer or repressor elements that would disrupt the function of the cardiac specific enhancer or repressor. One skilled in the art would not know how to use those nucleic acids without cardiac specific enhancer or repressor function based on the teaching of the specification. Therefore, these claims are not enabled.

Claims 18-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The nature of the invention is s nucleic acid comprising an enhancer element having 90%-95% sequence identity to SEQ ID NO:1, 2 and 3 or having 95% sequence identity to SEQ ID NO:1 & 2. The claims are not enabled for the same reasons discussed in the previous office action and in the above discussion.

Claim Rejections - 35 USC § 112 Second Paragraph

In response to the rejection of claims 1-12 of the term "substantially purified," Applicants argue that this term is clearly defined in the specification on page 12, thus this term is definite.

This argument has been considered but deemed unpersuasive. The definition in the specification does not address the question in the previous office action regarding the degree of the purity of the nucleic acid. Does it mean the nucleic acid molecule is isolated from the genomic DNA, for example, by restriction digestion? Applicants need to clarify the term encompasses. This rejection is maintained.

Claims 18 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18 and 20 recite the limitation "SEQ ID NO:3" in line 1. There is insufficient antecedent basis for this limitation in the claim because claim 1 does not have this limitation.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
March 10, 2003

Anne-Marie Falk